Interaction of benzothienoquinolines with DNA and lipid membranes monitored by fluorescence

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Benzothieno[3,2-*b*]quinoline **1** and benzothieno[2,3-*c*]quinoline **2** (Figure 1) are known for their anti-plasmodic and anti-infectious activities, acting mainly through intercalation between DNA base pairs when used in their salt form [1]. Normally synthesized by two separated reactions, our group was able to obtain the two compounds in a single reaction.

In this work, we present fluorescence studies of the interaction of compounds **1** and **2** with salmon sperm double-stranded DNA using spectroscopic techniques (Figure 1). These studies allowed to determine, through the McGhee and von Hippel modification of Scatchard plot, the binding constants, $K_i = (2.6\pm0.3)\times10^5\ M^{-1}$ for **1** and $K_i = (2.9\pm0.3)\times10^5\ M^{-1}$ for **2**, and binding site sizes in base pairs ($n = 21\pm6$ for **1** and $n = 7\pm2$ for **2**). Fluorescence quenching measurements using iodide ion showed that both compounds exhibit intercalation in DNA, compound **2** being the more intercalative one. Through the modified Stern-Volmer plots [2], the fraction of intercalated molecules was obtained: 31% for compound **1** and 42% for compound **2**.

Due to their potential biological activity, these benzothienoquinolines were encapsulated in liposomes of dipalmitoyl phosphatidylcholine (DPPC), dimyristoyl phosphatidylethanolamine (DMPE), egg yolk phosphatidylcholine (Egg-PC) and dioctadecyldimethylammonium bromide (DODAB). Fluorescence anisotropy measurements indicate that both compounds are mainly located in a hydrated and fluid environment, especially compound **1**. These studies may be important to future drug delivery applications of these potential biologically active compounds using liposomes, in order to reduce toxic effects or to increase the drug circulation time.

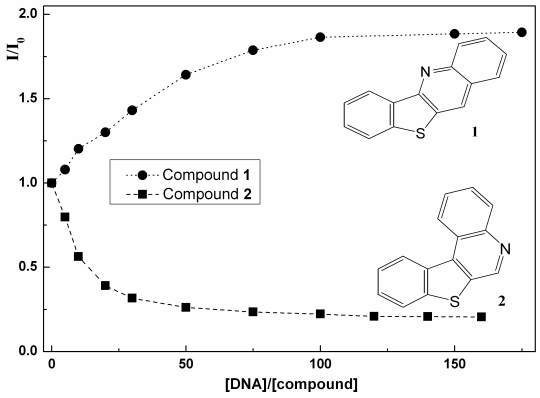

Figure 1. Fluorescence intensities ratio in the presence (I) and absence (I_0) of DNA for compounds **1** and **2** at several [DNA]/[compound] molar ratios.

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